UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,823	08/28/2002	Michel Revel	REVEL=16	1533

1444 7590 06/10/2003

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 06/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary	Application No.	Applicant(s)	
	09/980,823	REVEL ET AL.	
	Examiner	Art Unit	
	Fozia M Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's preliminary amendment canceling claims 1-4 and adding new claims 11-13, filed on 06 December 2001 in Paper No:6, is acknowledged. Thus claims 5-13 are pending and under consideration.

Claim rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 5-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 5-8 of the instant Application are drawn to a pharmaceutical composition comprising a chimera of interleukin-6 receptor and interleukin-6 (IL6RIL6). While claims 9-13 are drawn to a method of treating a neurological disease or disorder comprising administering said chimera. However, the specification as filed does not describe the structure of the IL6RIL6 chimera claimed in claims 5-8 or the structure of the chimera used in the method recited in claims 9-13. Therefore, conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention.

To satisfy the written description requirement, an applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the

claimed invention as of the date of invention. Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997); Hyatt v. Boone, 146 F.3d 1348, 1354, 47 USPQ2d 1128, 1132 (Fed. Cir. 1998). Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. Adequate written description requires more than a mere statement that it is part of the invention. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In the instant case, Applicant is claiming a chimera of IL-6R and IL-6 and a method of treating a disorder using said chimera, however, Applicants have not described the structure of said chimera.

Instant specification discloses that the claimed chimera is a recombinant glycoprotein obtained by fusing the entire coding sequence of the naturally occurring human soluble interleukin-6 receptor δ-val to the entire coding sequence of mature naturally occurring IL-6, (page 7, lines 19-28). However, instant specification does disclose the structure of said chimera. With respect to claims 9-13, instant specification does not disclose the structure of the chimera used in the claimed method. One of

ordinary skill in the art would not be able to visualize the claimed chimera. Instant specification asserts that chimera claimed in instant application is preferably produced in mammalian cells as described in WO 99/02552 world patent. However, there are several IL6RIL6 chimeras described in WO 99/02552, (see pages 7-8). One of the chimeras disclosed in WO 99/02552, is obtained linking the C-terminal Val-356 of the soluble IL-6 receptor to the N-terminal Pro-29 of IL-6 through a linker peptide, which comprises 3 amino acid residues. In another chimera disclosed in the world patent, the linker peptide is 13 amino acid residues long. WO 99/02552 also discloses various linker peptides and various IL-6R IL-6 chimeras generated using different linker peptides, the structure of one of these chimera is on Figure 11 and SEQ ID NO:8 of WO 99/02552. Therefore, one of ordinary skill in the art would not know from the instant disclosure, whether the claimed chimera is obtained by fusing the soluble IL-6R to IL-6, and if so whether a linker peptide is used.

Therefore, it does not appear that the inventor was in possession of a pharmaceutical composition comprising a chimera of interleukin-6 receptor and interleukin-6 (IL6RIL6).

2b. Claims 5-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention.

Claims 5-8 of the instant application encompass a pharmaceutical composition comprising a chimera of interleukin-6 receptor and interleukin-6 (IL6RIL6). Thus the

claims encompass a "pharmaceutical use" for the composition. For the claim to be enabled, the specification must teach how to use the composition for at least one therapeutical use without undue experimentation. Steadman's Medical Dictionary (24th Edition, 1982) defines "drug" as "a therapeutic agent; any substance other than food, used in the prevention, diagnosis, alleviation, treatment or cure of disease in man and animal." Ansel et al. (Pharmaceutical Dosage Forms and Drug Delivery Systems, Seventh Edition), says "A drug is defined as an agent intended for use in the diagnosis, mitigation, treatment, cure or prevention of disease in humans or in other animals. One of the most astounding qualities of drugs is the diversity of their actions and effects on the body." The following are examples of "pharmaceutical uses": administering vitamin supplements (preventing disease); using labeled antibodies for in vivo imaging (diagnosing disease); administering a substance to alleviate a symptom of a disease (alleviating or treating disease); and administering an antibiotic (curing bacterial infection). Administering a polypeptide to produce antibodies to protect the individual from contracting a disease, i.e., vaccination, is a pharmaceutical use, however, administering a polypeptide to produce antibodies which are then collected from the animal and used in various ways is not a pharmaceutical use.

In the present situation, to enable a pharmaceutical use for the claimed chimera requires the specification to teach how to use the substance, without undue experimentation, for the prevention, diagnosis, alleviation, treatment or cure of a disease in the animal to which the substance is administered. The specification asserts that the chimera of the instant invention is useful in the treatment and and/or prevention

of neurological diseases or disorders, (page 4, lines 28-29). However, the specification does not provide adequate guidance as to how the claimed chimera can be used to treat or prevent any disorder.

Claims 9-13 of the instant Application are drawn to a method of treating a neurological disease or disorder comprising administering an effective amount of ILR6IL6 chimera. The claims recite multiple sclerosis, Alzheimer's disease, Parkinson's disease and ALS as the disorders that can be treated using the chimera of the instant application. However, the specification as filed does not disclose or describe one single method in which of any of the recited diseases or disorders have been treated using the IL6RIL6 chimera of the instant invention. Thus the specification is non-enabling for the method claimed in claims 9-13. There are no examples of treatment by administration of the claimed chimera. There are a number of in vitro experiments showing that the IL6RIL6 chimera has direct effect on myelin gene transcription in committed Schwann cells, (see Example 1, on pages 12-14). The specification also discloses that IL6 chimera inhibits oligodendrocyte proliferation by 40 to 50% compared to controls, (see Example 2). However, most of the examples in the instant application are directed to determining the functions and activities of the IL6RIL6 chimera in differentiation and myelination of myelinating cells. Example 8 of the instant specification uses a murine model of chronic relapsing multiple sclerosis, however, this example does not demonstrate whether IL6RIL6 chimera improves the clinical score of these mice.

Therefore, it is not predictable from the experiments of the instant specification or from the teachings of the prior art that the IL6RIL6 chimera is effective in treating the recited disorders.

Due to the lack of direction or guidance in the specification, the absence of working examples and teachings of the prior art, the unpredictability in the art, and the complex nature of the invention, undue experimentation would be required of the skilled artisan to practice the method of treating neurological diseases or disorders, such as multiple sclerosis, Alzheimer's disease, Parkinson's disease and ALS, said method comprising administering an effective amount of ILR6IL6 chimera. Furthermore, there is no guidance as to how much is effective to treat any of the recited disorders. Also "prevention" encompasses determining in advance if a patient is susceptible to multiple sclerosis, Alzheimer's disease, Parkinson's disease or ALS disorder, however Applicants are not enabled for such.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3a. Claims 5-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3b. Regarding claims 5-6, 9-11, the phrase "optionally" renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

3c. Claims 6, 7, 8, 10, and 11 recite the acronyms "CNS, PNS, MS and ALS, ", however, these acronyms make the claims unclear. Reciting the full name of these abbreviations in the first independent claim would obviate this rejection.

Claims 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, insofar as they depend on claim 11 for the limitations set forth directly above.

Claim rejections-35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4a. Claims 5-8 are rejected under 35 U.S.C § 102(b) as being anticipated by Revel et al (WO 99/02552, 01/21/1999).

Revel et al disclose a pharmaceutical composition comprising a chimera of glycosylated soluble interleukin-6 receptor and interleukin-6, (sIL-6R/IL-6), (pages 7-8 and page 11, lines 21-28).

It does not appear that the intended use language recited in claims 5-8 results in a structural difference of the claimed chimera when compared to the prior art disclosure.

Therefore, Revel et al reference anticipates instant claims 5-8 in the absence of any evidence to the contrary.

Conclusion

5. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday, 6:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4227 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Exmainer
Art Unit 1647
June 10, 2003

Gary L. Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600